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ORIGINAL RESEARCH

A study on HbA1Cand serum uric acid levels inpatients with psoriasis in Kashmiri population- A Pilot study

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ABSTRACT

Background:Psoriasis is a chronic immune-mediated skin disease that affects 125 million people worldwide, which is 2 to 3 percent of total population. Psoriasis is a common, chronic, inflammatory disease that is associated with an increased risk of cardiovascular, metabolic, and renal disease in a manner that varies with psoriasis severity and is often independent of traditional risk factors.

Aim: To study the association of HbA1C and uric acid with psoriasisin the Kashmiri population.

Method: A total of 70 cases, diagnosed for psoriasis were undertaken during the study period December 2018 to February 2021 from the department of Dermatology in the test group. An equal number of age and sex matched healthy individuals with no skin disease were taken as control group. Blood samples were collected and analysed in the laboratory of department of Biochemistry, Government Medical College, and Srinagar. All study participants provided written informed consent prior to enrolment.

Results:Psoriatic patients had higher levels of HbA1c (5.3 ± 0.09 vs 4.9 ± 0.063 mg/dl; P=0.005) and significantly greater prevalence of hyperglycemia (24.2% vs 12.8%; P=0.009) than individuals without psoriasis. Prevalence of pre diabetes and diabetes in patients with psoriasis was 11.1 % and 14.2 % respectively as compared to controls.Multivariate logistic regression analysis showed that psoriasis can be a strong predictor of hyperglycemia (odds ratio 2.14; 95% confidence interval 0.939-4.903; P=0.001). Patients with psoriasis also had significantly higher levels of serum uric acid than controls. Mean serum uric acid in cases was 6.13 ± 0.187 and in controls it was 5.56 ± 0.123 with p value<0.05.

Conclusion: There was a significant increase in Hba1c levels in patients with psoriasis than control. In addition, we found increased level of serum uric acid in patients with psoriasis than control. There was a positive correlation between HbA1c values and higher BMI.

INTRODUCTION

Psoriasis is a genetically determined immune-mediated inflammatory disease mediated by T helper cells. It is reported that Psoriasis affects individuals in their third or fourth decades equally affecting both the genders.[1]

It is reported that one in three people with psoriasis may develop psoriatic arthritis. Worldwide 125 million people suffer from psoriasis, which is 2 to 3 percent of total population[2].The symptoms of Psoriatic arthritis include swelling, stiffness and pain in joints or area surrounding the joints. Other clinical manifestations of Psoriasis are appearance of erythematosquamous papules or plaques of various sizes over the knees, elbows, genital area, scalps and body. Psoriasis is now seen as a systemic disease with associated comorbidities[2]. The appearance of comorbidities correlates with the severity of the clinical presentation, and their number usually increases with age and disease duration. Psoriasis, with other chronic inflammatory systematic diseases like systemic lupus erythematosus and rheumatoid arthritis, may be linked to increased cardiovascular disease risk because of common pathogenic mechanisms.Aortic arterial stiffness is a moderate predictor of cardiovascular disease in patients with psoriasis vulgaris[3].High serum uric acid and elevated HbA1c are both associated with metabolic syndrome.

It is reported that high levels of serum uric acid (SUAC) are frequently detected in patients with psoriasis[4].Psoriasis has been correlated with increased uric acid concentration as per report of arthritis foundation[5,6,7].Uric acid is the end product of purine metabolism and normal serum uric acid values range from 1.5 to 6.0 mg/dl in adult females and from 2.5 to 7.0 mg/d in adult males [14, 15]. High cell turnover in the epidermis can lead to hyperuricemia in psoriasis patients.The rapid epidermal turnovers cause an increase in the purine breakdown , thus altering the serum uric acid level[5].Certain studies conducted in Israel,Germany and Russia have showed an association between hyperuricemia and psoriasis.[6, 7, 8].HbA1c is a glucose bond with haemoglobin. HbA1c describes the average blood glucose concentration for three months. Miller et al suggested that psoriasis increases the risk of diabetes. In another meta-analysis OR for association betweenT2DM and psoriasis was 1.76 (95% CI 1.59–1.96)[9].Chronic inflammation causes releaseof pro-inflammatory molecules leading to one or more associated disorders, such as atherogenesis and atherosclerosis, insulin-resistance, hypertension, obesity, dyslipidemia, metabolic syndrome, and type 2 diabetes mellitus.

HbA1c canbe used as an objective measurement to detect the occurrence of insulin resistance. The purpose of this study was to prove the correlation between psoriasis vulgaris withHbA1c and uric acid in the Kashmiri population.

METHODOLOGY

A cross sectional observational study was carried out at Government Medical College Srinagar J & K. A total of around 70 cases, diagnosed for psoriasis were undertaken during the study period December 2018 to February 2021 from the department of Dermatology in the test group. An equal number of age and sex matched healthy individuals with no skin disease were taken as control group. Blood samples were collected and analysed in the laboratory of department of Biochemistry, Government Medical College, and Srinagar. All study participants provided written informed consent prior to enrolment.

STUDY POPULATION

The study consisted of 70 diagnosed patients of psoriasis within the age group of 18 to 65 years and 70 normal subjects in the same age group.

INCLUSION CRITERIA

All patients attending the Dermatology out-patient department, Government Medical College Srinagar who were diagnosed with psoriasis were included in the study. Both male and female patients within the age group of 18-65 years were included

EXCLUSION CRITERIA

The following patients were excluded from the study.

- Previous history of hypertension
- Diabetes Mellitus
- Renal disease
- Thyroid disorder
- Dyslipidemia
- Liver disorders and other chronic disorders affecting the parameters under study
- Chronic smokers and alcoholics
- Psoriatic patients receiving any systemic treatment for at least 4 weeks or photochemotherapy within 3 months before enrolment and patients who did not give voluntary informed consent for reviewing, patients less than 18 years and more than 65 years were excluded from the study.

CONTROLS

An equal number of individuals without history of any kind of skin disease were selected who included both males and females in the age group of 18 to 65 years.

Height and weight of the individuals was obtained following standard protocol and instrument. Height was measured using a stadiometer and weight by a weighing scale.

BMI was calculated as per formula: Weight (Kg)/Height (meter)^2.

Approval of the institutional ethics committee was obtained before starting the study

RESULTS

In this study,we selected 70 patients (34 were females and 36 were males) and 70 control subjects (34 were Male, 36 were females). The mean age of patients with psoriasis and controls was 43 ±1.18 and 42.42 ±1.18 years. The mean BMI of patients and control were 24 ±0.2 and 23.28 ± 0.15.

	Controls Mean ± SE	**Confidence Interval level 95(%)**	**Patients with psoriasis ± SE**	**Confidence Interval level 95(%)**	**p-value**
Fasting glucose (mg/dl)	91± 0.8	1.777549833	104 ± 2.01	4.017072453	< 0.005
HbA1c (%)	4.9 ± 0.63	0.126705828	5.3 ± 0.09	0.182769914	< 0.005
Uric Acid (mg/dl)	5.56± 0.123	0.247400138	6.13 ± 0.187	0.362645143	<0.05

Table 1 Shows Mean ± S.E of Fasting glucose, HBA1c and uric acid T-test shows prevalence of (p< 0.05)

Psoriatic patients had higher levels of HbA1c with mean value (5.3% ± 0.09, P=0.018) and significantly greater prevalence of hyperglycemia (24.2% vs 12.8%; P=0.009) than individuals without psoriasis. Psoriatic patients were found to have higher levels of serum uric acidthan controls with p value<0.05. The mean ± S.E of Uric acid in patients and control is 6.13 mg/dl and 5.56 mg/dl respectively. T test prevalence shows (P<0.05) a shown in table 1.

CORRELATION MATRIX

	HbA_1c	BMI	Fasting Blood Glucose
HbA_1c	1.00000	0.581101	0.812840
BMI	0.581101	1.000000	0.518077
Random Blood Glucose	0.812840	0.518077	1.00000

Table 2 showing correlation matrix in patients

Correlation matrix shows that Psoriatic patients have strong correlation with hyperglycaemia than control.R^2 is equal to 0.695695, it means the predictor Xi explains 69.6% of variance of Y. In this case the coefficient of multiple correlation R is equal to 0.834083, which means that there is a very strong direct relationship between the predicted data and observed data.We found negative correlation between age and Hba1c i.e. -0.212585 we also found negative correlation ship between BMI and Age of patients. Therefore,the followingindependent variable is not significant as predictors for Y: X.Soit was excluded from the model.

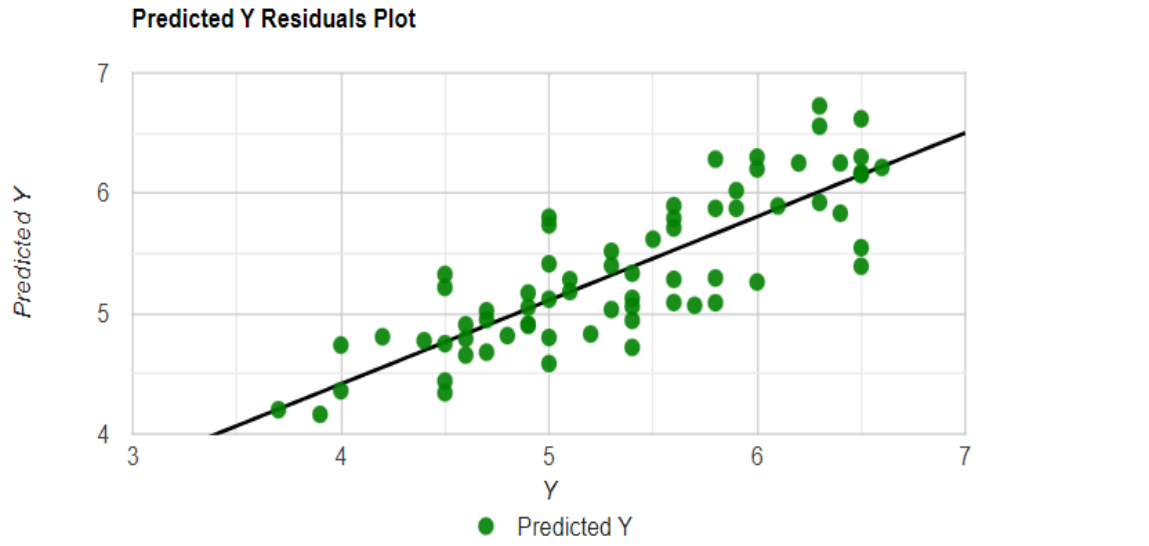
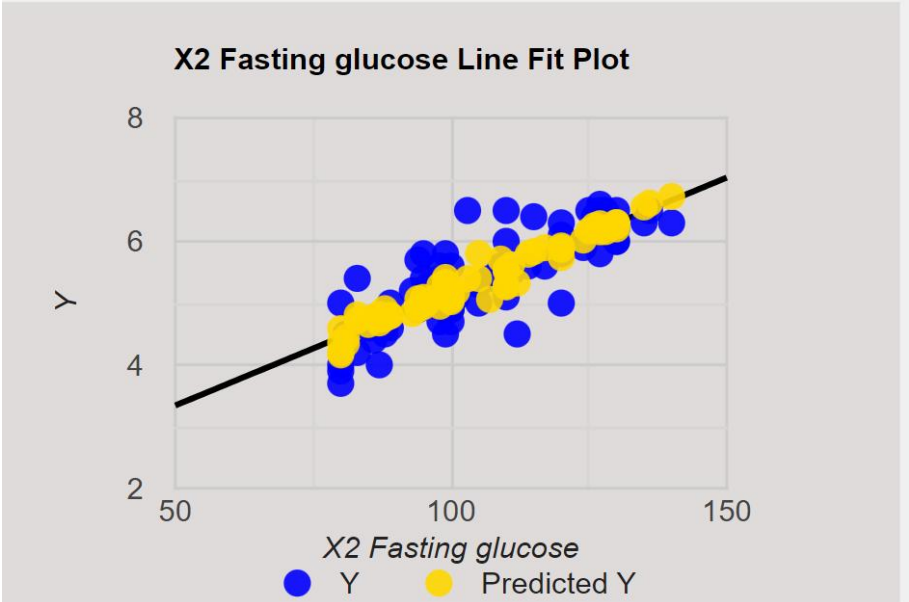


Fig.1 shows predicted Y residual plot between independent values and dependent values in psoriatic patients.


X2 Fasting glucose Line Fit Plot
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6
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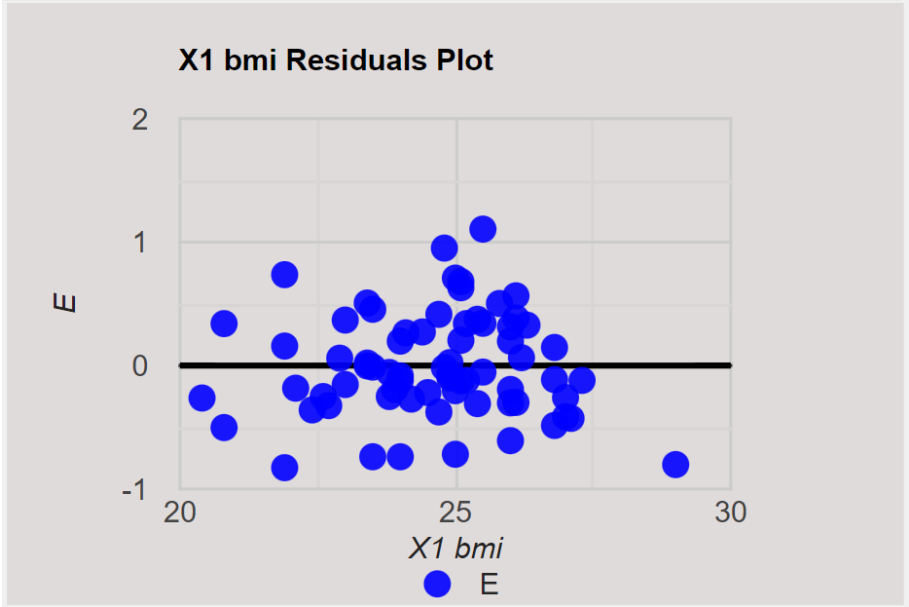
150
X2 Fasting glucose
Y
Predicted Y


X1 bmi Residuals Plot
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X1 bmi
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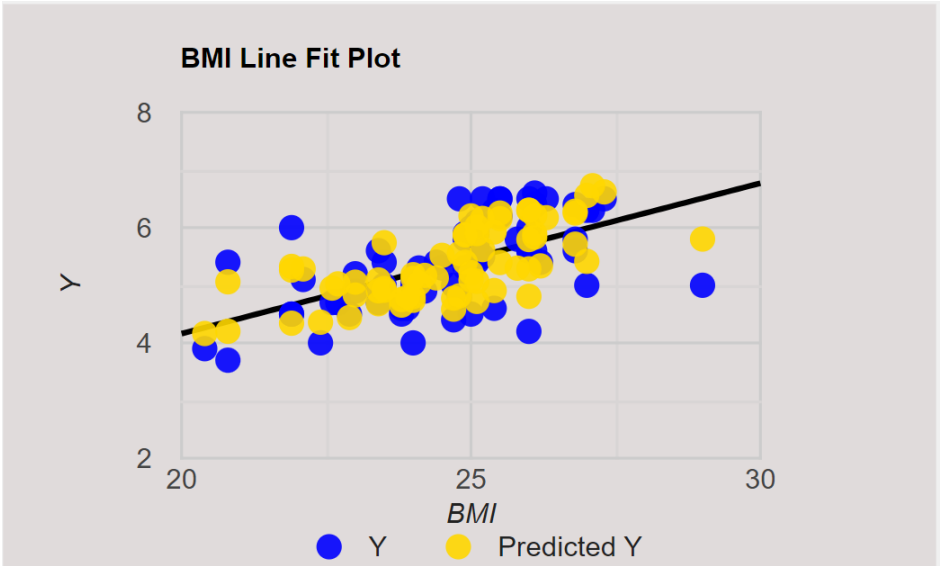
BMI Line Fit Plot
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6
4
2
Y
20
25
30
BMI
Y
Predicted Y

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Figure 2 shows line fit plot, (a) between Blood glucose and HBA1c, (b) between BMI and HbA1c. in psoriatic patients

When linear regression line was drawn between BMI and Hba1c of psoriatic patients we found R Square (R)equals 0.3377. It means that 33.8% of the variability of Y is explained by X.It means that there is a moderate direct relationship between X and Y. The results of the Pearson's correlation indicated that there is a significant large positive relationship between HbA1c and BMI. r (70)=0.581, p< 0.001).

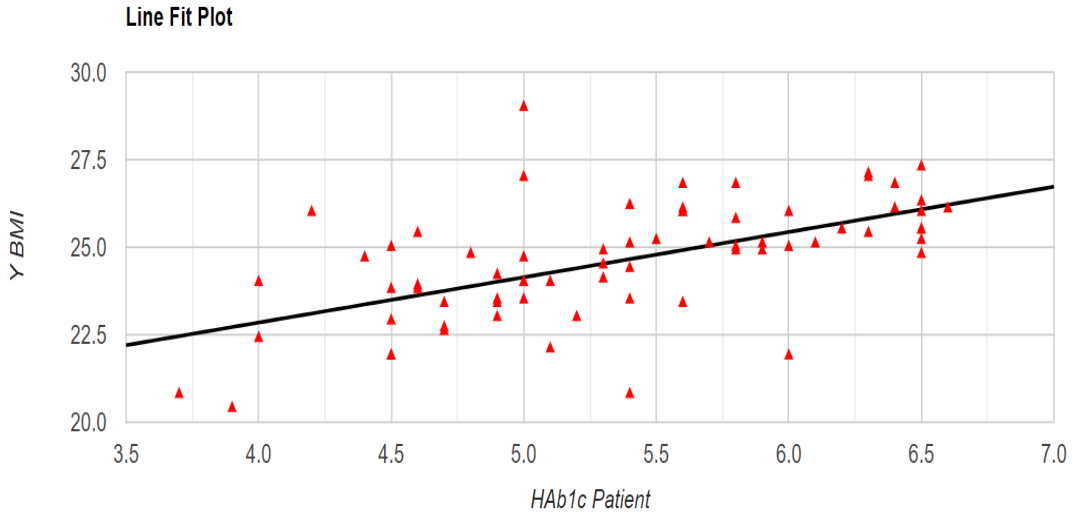

Fig 3 shows line fit plot between BMI and HbA1c in psoriatic patients.

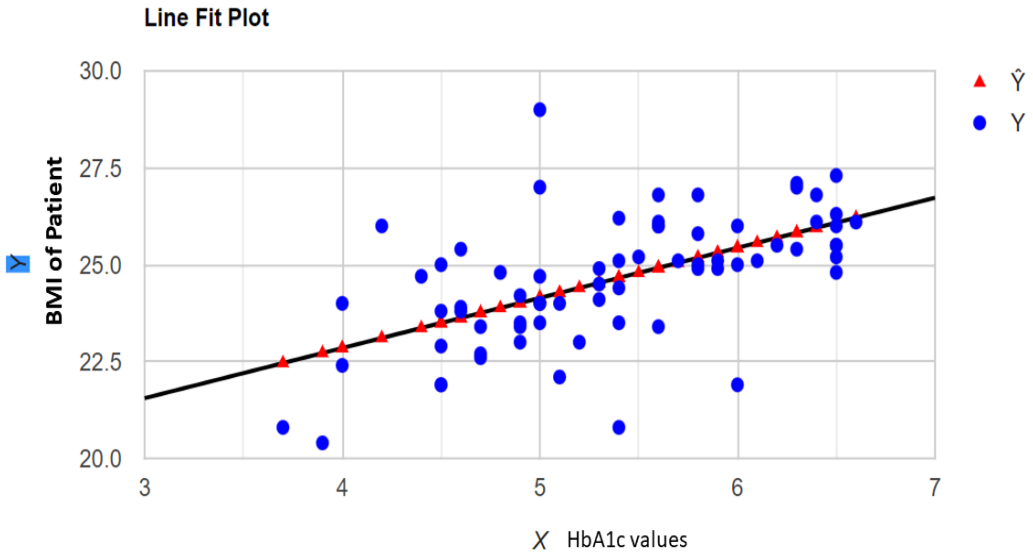

Fig 4.Regression line BMI, HBa1c in Psoriatic Patients

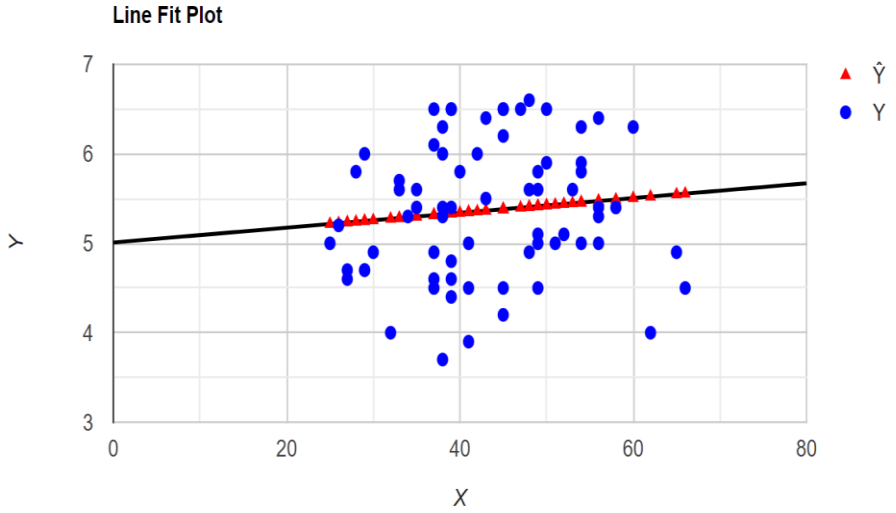

Fig 5 shows line fit plot between Age and HBA1c in psoriatic Patients.

CORRELATION MATRIX

	HBA_1c	Age	BMI
HBA_1c	1.00000	-0.124957	0.347521
Age	-0.124957	1.000000	-0.133147
BMI	0.347521	-0.133147	1.00000

Table 3.correlation matrix in control individuals

The coefficient of multiple correlation (R) equals to 0.347521 in non-psoriatic individuals showed weak direct relationship between predicted data (ẏ) and the observed data (y). R square (R^2) equals 0.120771. It means that the predictor (X_i) explains 12.1 % of variance of Y.

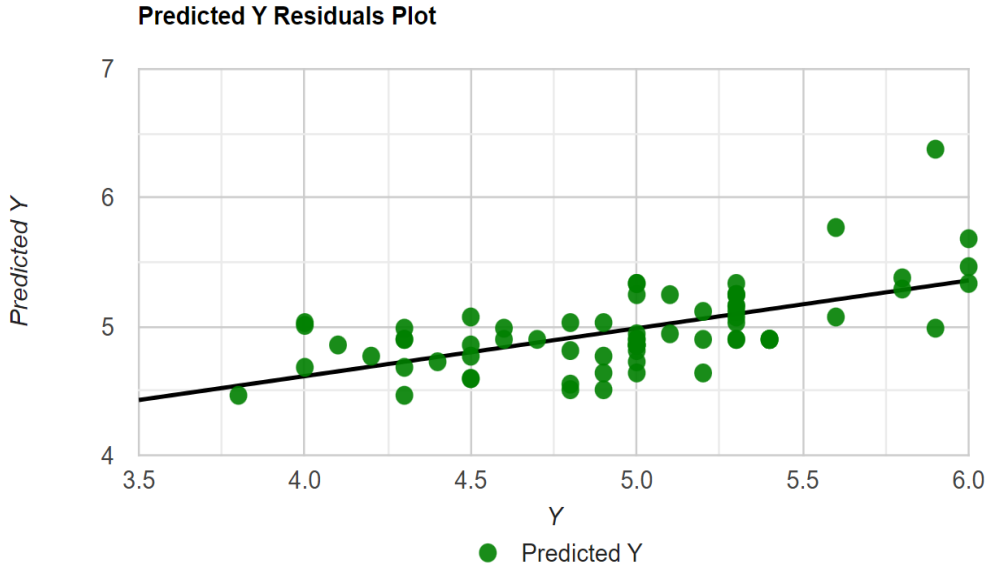

Figure 6 Predicted Y residual plot in Control individuals

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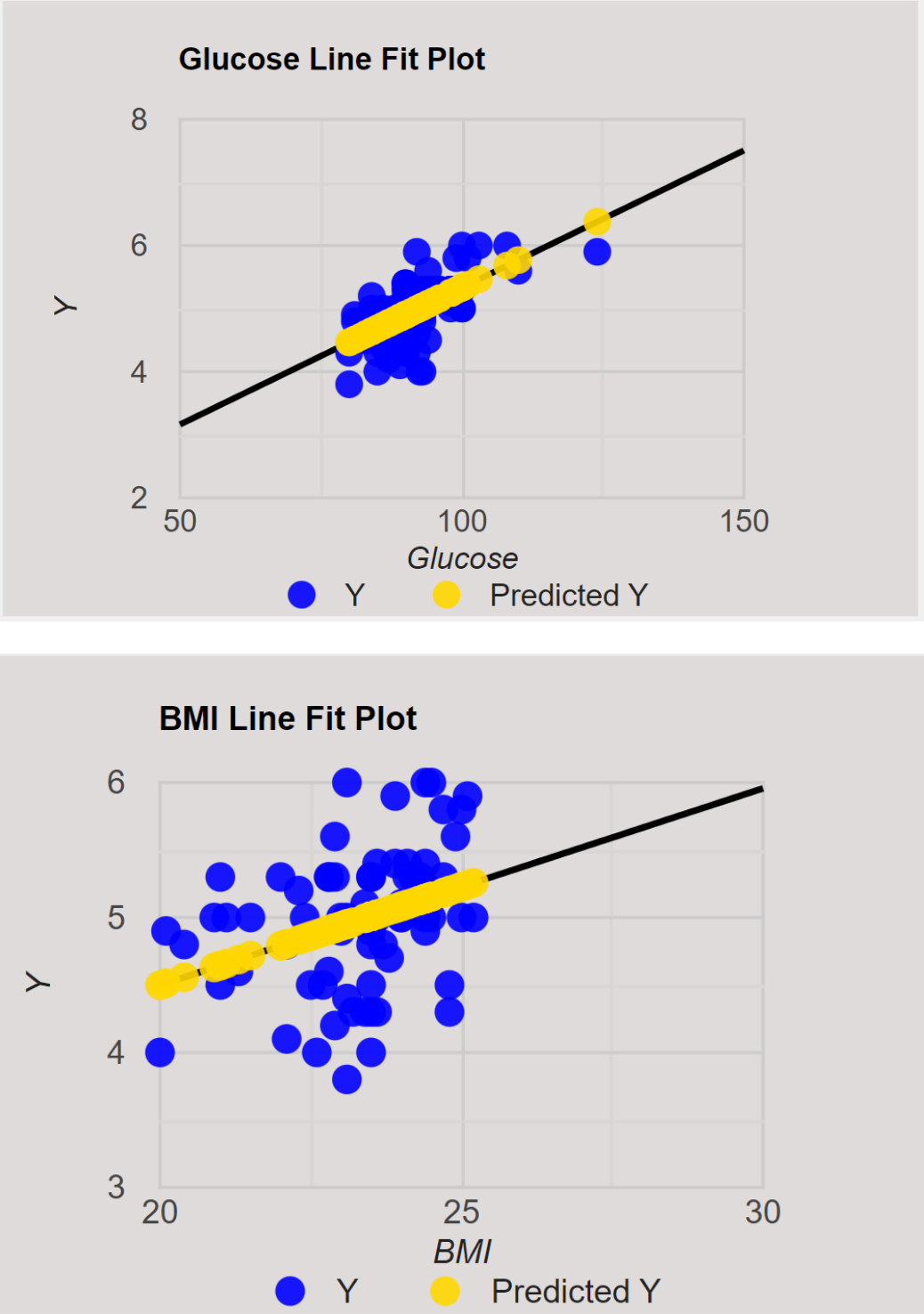

Figure 7 Line fit plot of control individual glucose and BMI with HbA1c values

In control individuals Pearson's correlation indicated that there is an insignificant negative relationship between X Hba1c and Age (r(68)= 0.125, p =0.303. the difference between the correlation of the sample and the expected correlation is not big enough to be statistically significant.In control individuals the results of the pearson'scorelation indicated that there is significant medium positive relationship between HbA1c values and BMI with R =0.348 and p=0.003

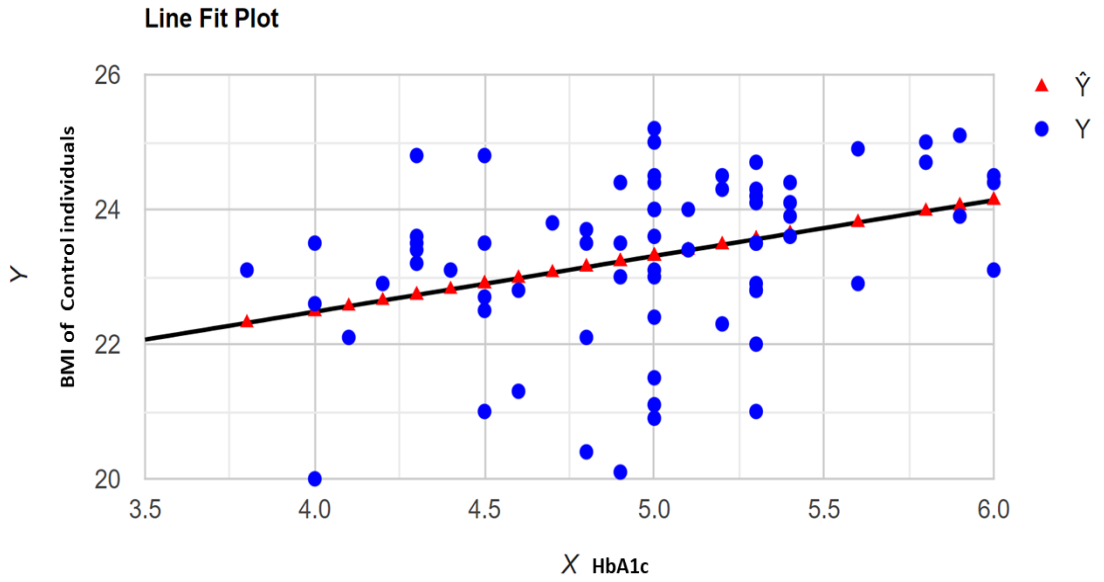

Figure 8 Linear regression line in control individual BMI and HbA1c

R Square (R^2) equals 0.1208. It means that 12.1% of the variability of BMI is explained by HbA1c. Correlation (R) equals 0.3475. It means that there is a weak directrelationship between BMI and HbA1c in control individuals. These findings underscore the importance of screening for glycaemic and uric acid abnormalitiesand to mitigate CV disease risk in patients with psoriasis.

DISCUSSION

Patients with moderate to severe psoriasis are having prevalence of a cluster of metabolic disorders including obesity, impaired fasting glucose/ diabetes, dyslipidemia and hypertension. The association between psoriasis and diabetes may be due to a lot of factors including common genetic background. The study was planned to find the correlation of psoriasis with glycaemic control and serum uric acid levels.We found that the mean HbA1c level was significantly higher in patients with psoriasis than control table 1.The correlation matrix shows that Psoriatic patients have strong correlation with hyperglycaemia than control (table 2). In this case the coefficient of multiple correlation R is equal to 0.834083, which means that there is a very strong direct relationship between the predicted data and observed. However, we found weak direct relationship between predicted data (ỳ) and the observed data (y) in case of control individual's (table 3,figure 4).When linear regression line was drawn between BMI and Hba1c of psoriatic patients there is a moderate direct relationship between BMI of patients and HbA1c values of patients figure as compared to control individuals where weak direct relationship between BMI and Hba1c values was observed as shown in figure 6. The results of the Pearson's correlation indicated that there is a significant large positive relationship between HbA1c and BMI. r (70)=0.581, p< 0.001) table 2 .

Increased chemerin and leptin and reduced adiponectin serum have been reported in patients with psoriasis compared to age, sex and BMI matched controls[19,11,12]. Obesity is a strong risk factor for insulin resistance and diabetes[13]. In our study, we also observed direct relationship between BMI and raised blood glucose asPearson's correlation indicated a significant large positive relationship between HbA1c and BMI in psoriatic patients than control individuals. WhereasPearson'scorelation between HbA1c and BMI in case of control showed significant medium positive relationship with R =0.348 and p=0.003. Our results highlight the importance of glucose homeostasis in patients with psoriasis by showing the correlation between psoriasis and HbA1c levels.

The hypothesis that psoriasis itself constitutes a pre-diabetic condition has been suggested by the study of Gyldenløve et al. conducted over 32 patients with psoriasis [14].
Serum uric acid (SUA) mediates inflammatory pathways via the secretion of proinflammatorychemokines. Interestingly,it has been also known to act as a potential antioxidant in patients with psoriasis. We found that the mean serum uric acid level in psoriatic individuals was significantly higher (6.13 mg/dl) than non-psoriatic individuals (5.53 mg/dl). Emrah et al have also reported the same mean value of uric acid values as we have reported in this study[15]. However, we found an insignificant negative relationship between uric acid and HBA1c values on Pearson's correlation. Eisen and Seegmiller et al postulated that the rise in serum uric acid levels in patients with psoriasis was due to the increased cell turnover in the skin[16]. It is thus conceivable that several underlying mechanisms are involved in the association between psoriasis and metabolic syndrome that lead to altered glucose and uric acid metabolism.MonitoringHbAIcand serum uric acid levels in patients with psoriasis can aid in delaying/prevention and early diagnosis of Diabetes and other metabolic disorders like gout etc. This can further alleviate early occurrence of complications of diabetes as well. Our results indicate that higher HbA1c and serum uric acid levels are associated with psoriasis. Thus, patients of psoriasis should be encouraged to exercise regularly, have a healthy diet and monitor their blood glucose and serum uric acid levels. Insulin-resistance seems to be the keystone of psoriasis comorbidities. Psoriasis reinforces diabetes, causing a greater cardio-metabolic risk. Regular and early monitoring of serum uric acid levels can help in preventing and in correct differential diagnosis of psoriatic arthritis as well.

CONCLUSION

We found a direct relationship of psoriasis with hyperglycemia and hyperuricemia in the Kashmiri population. There was a significant increase in Hba1c levels in patients with psoriasis than control. In addition, we found increased level of serum uric acid in patients with psoriasis than control. There was a positive correlation between HbA1c values and higher BMI. In all, our observations throw light on the various intersecting factors that reinforce that psoriasis is infact a multisystemic disorder with increased risk of metabolic syndrome, diabetes, gout and cardiovascular diseases. A limitation of our study is the small sample size. More trials and researches are warranted to establish the relationship between hyperglycaemia, hyperuricemiaand psoriasis.

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